Post-hoc analysis of the LIGHTHOUSE and SPOTLIGHT studies to assess the impact of urinary activity on interpretation of ^{18}F-flotufolastat PET/CT

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Introduction and overall goal: Radiohybrid (rh) ^{18}F-flotufolastat (^{18}F-rhPSMA-7.3) is a novel high affinity prostate-specific membrane antigen (PSMA)-targeting positron emission tomography (PET) radiopharmaceutical recently approved by the United States Food and Drug Administration as a diagnostic imaging tool for patients with prostate cancer.

Specific aims: To conduct a post-hoc analysis of all ^{18}F-flotufolastat scans acquired within two Phase 3 studies of the diagnostic performance of ^{18}F-flotufolastat, in order to assess the impact of urinary tract activity of ^{18}F-flotufolastat on disease assessment.

Rationale and background: Early clinical data[1] show ^{18}F-flotufolastat to have lower average urinary excretion compared with other renally-cleared PSMA-PET agents and thus potential for improved image evaluation in the prostate and peri-ureteric regions.

Methods and materials: Men with either treatment-naïve, newly diagnosed, unfavorable intermediate to very high-risk prostate cancer or recurrent prostate cancer were enrolled in LIGHTHOUSE (NCT04186819) and SPOTLIGHT (NCT04186845), respectively. All patients underwent PET/computed tomography (CT) 50–70 min after intravenous administration of 8 mCi (296 MBq) ± 20% ^{18}F-flotufolastat. For the present analysis, 718 ^{18}F-flotufolastat scans (352 from LIGHTHOUSE and 366 from SPOTLIGHT) were re-evaluated by 3 trained readers with 13–25 years' nuclear medicine experience. Reader 1 performed a quantitative assessment (SUV_{max} and SUV_{mean}) of bladder activity in a circular region-of-interest over the maximum diameter of the bladder activity in the transverse plane. All 3 Readers performed a qualitative assessment of the impact of any urinary activity on assessment of the prostate/bed and pelvic/retroperitoneal lymph nodes using a 3-point scale (0 = no/minimal visible urinary activity, 1 = urinary activity visible but distinction between urine and disease possible and 2 = assessment inhibited by urinary activity). Further qualitative assessments on the presence or absence of ureteric activity (defined as a stasis of urine in the ureter visualized on the MIP at viewing window level 0–10) and halo artifacts (defined as a gross photopenic region around bladder extending significantly beyond the bladder and overlaying other structures of the pelvis as visible on transverse slices) were also conducted by all 3 readers.

Results: Of the 718 eligible scans, 712 (348 newly diagnosed and 364 recurrent prostate cancer) were evaluable for bladder activity. Reasons for exclusion were cystectomy, renal failure, or urinary catheter *in situ* (n=2 each). The median bladder SUV_{max} and SUV_{mean} were 17.1 and 12.5, respectively.

Qualitative assessments by the 3 readers show that between 616 and 694 of the 712 patients (87–97%) were scored 0 or 1 as the reader determined there was no potential difficulty distinguishing between urinary activity and disease. In a minority of patients (2.5–13%, 18–96/712), the assessment was inhibited by urinary activity (score=2). By majority read, 11%, 85% and 3.4% were scored 0, 1 or 2, respectively. When using the SUV data from Reader 1's quantitative assessment, the patients scored 2 (n=24, 3.4% by majority read), were noted to have a higher median bladder SUV_{mean} (20.5) than those scored 0 (3.8) or 1 (14.0).

Ureteric activity was reported in 253–369 (36–52%) patients. Halo artifacts that could potentially inhibit assessment around the bladder rarely occurred, with the readers reporting 0–27 occurrences among the 712 scans (0–3.8%; 2 [0.3%] by majority read).

Discussion and conclusion: Data from this post-hoc analysis of ^{18}F-flotufolastat scans from two prospective phase 3 trials show that the urinary activity of ^{18}F-flotufolastat is relatively low and does not influence disease assessment for the vast majority of patients. Halo artifacts inhibiting disease assessment also occurred very rarely. Moreover, while this study was not designed as a head-to-head comparison, the median bladder SUVs compare favorably with values reported in the literature for other renally excreted PSMA-PET ligands.[2–5]

References: 1. Tolvanen et al. *J Nucl Med*. 2021;6(5):679–84; 2. Giesel et al. *J Nucl Med*. 2018;59(7):1076–80; 3. Donswijk et al. *EJNMMI Res*. 2022;12:42; 4. Uprimny et al. *EJNMMI*. 2021;48,123–33; 5. Kuten et al. *J Nucl Med*. 2020;61.4:527–32.